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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/712,821	11/13/2000	Todd M. Kinsella	A-70036/RMS/JJD	9149
959	7590	01/10/2005	EXAMINER	
LAHIVE & COCKFIELD, LLP. 28 STATE STREET BOSTON, MA 02109			PONNALURI, PADMASHRI	
			ART UNIT	PAPER NUMBER
			1639	

DATE MAILED: 01/10/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>
	09/712,821	KINSELLA, TODD M.
	Examiner Padmashri Ponnaluri	Art Unit 1639

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) Responsive to communication(s) filed on 06 July 2004.
- 2a) This action is FINAL.                    2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) Claim(s) 7-13 and 15-45 is/are pending in the application.
- 4a) Of the above claim(s) 7-12 is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 13 and 15-45 is/are rejected.
- 7) Claim(s) 30 is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All    b) Some \* c) None of:
  1. Certified copies of the priority documents have been received.
  2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | Paper No(s)/Mail Date. _____  |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
|  | 6) <input type="checkbox"/> Other: _____                                    |

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**DETAILED ACTION**

1. The amendment and response filed on 7/6/04 has been fully considered and entered into the application.
2. Claim 14 has been canceled and claims 13, 15, 17, 20, 34 have been amended by the amendment filed on 7/6/04.

(The preliminary amendment filed on 5/10/02 has canceled claims 1-6, and added new claims 13-37. Amendment filed on 2/5/03 has amended claims 19, 21-22, 24-25, 27, 30-33, and added new claims 38-45.)

Accordingly claims 7-13, 15-45 are currently pending in this application.

3. Claims 7-12 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 9.
4. Claims 13, 15-45 are currently being examined in this application.

*Priority*

5. This application claims priority to provisional application 60/165,189 filed on 11/12/99.

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application); the disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The instant Patent application (09/712,821) specification is not same as the priority provisional application specification. For example the provisional application specification has not disclosed the instantly claimed expression vector combination. The provisional application has not disclosed expression vectors with HBEGF. Further the newly incorporated subject matter of US Patent application 09/710,058 was not present in the provisional application specification. Thus, the instantly claimed invention gets the effective filing date of the instant application filing date 11/13/00.

***Drawings***

6. The drawings filed on 11/13/00 have been objected. Applicants are requested to see the PTO 948 attached to the previous office action mailed on 6/4/02.

***Specification***

7. The amendment to the specification to correct the US patent application number has been fully considered and entered into the application.

***Withdrawn Claim Rejections***

8. The new matter rejection of claims 34, 35, 36 and 45 has been withdrawn in view of applicant's response pointing support for the limitations.

9. The objection to claim 34 has been withdrawn in view of amendments to the claim.

10. The rejection of claim 28 as being anticipated by US Patent 6,613,563 B1 (Sosnowski et al) has been withdrawn.

11. The rejection of claims 13-32, 37-44 as being anticipated by US Patent 6,465,253 B (Wickham) has been withdrawn in view of the amendment.

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12. The rejection of claims 13-33, 37-44 over US 2002/0168649 and US Patent 6,465,253 B1 has been withdrawn, in view of the filing date of the instant application (after September 1999).

13. The lack of written description rejection of claims 18, 23, 32 and 34-36 and 45 has been withdrawn in view of new rejections.

#### *Claim Objections*

14. Claim 30 is objected to because of the following informalities: claim 30 improperly depends on claim 31. Appropriate correction is required.

#### *New Claim Rejections*

15. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

16. Claims 25-37 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The amendment filed on 5/10/02 introduced new claims.

The newly added (5/10/02) independent claim 25 recites expression vector comprising from 5` to 3`: HBEGF, a 2a site, nucleic acid encoding GFP, an IRES site, and a promoter of interest.

The newly added (5/10/02) independent claim 28 recites expression vector comprising from 5` to 3`: HBEGF, an IRES site, and a promoter of interest.

The newly claimed limitations ‘an expression vector comprising from 5` to 3`...’ claimed in Claims 25-37 has no clear support in the specification and the claims as originally filed. The figure 18 A, or B shows that the promoter is attached to HBEGF. And figures 18 C-G do not even show the promoter. The figures 18 A-G do not show the direction either 5 to 3` or 3` to 5`. In the absence of guidance in the specification, it has been considered that figure 18 A-G are read as 5` to 3`. Thus, according to figures 18 A-B, the vectors have from 5` to 3`: CD9-IRES-GFP-HBEGF-promoter, which is opposite of what is instantly claimed. The specification has not disclosed the instantly claimed vectors. The subject matter claimed broadens or alters the scope of the invention as originally disclosed in the specification.

If applicants disagree, applicant should present a detailed analysis as to why the claimed subject matter has clear support in the specification.

17. Claims 13, 15-45 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The instant independent claim 13 recites an expression vector comprising, a nucleic acid encoding HBEGF, a nucleic acid encoding GFP, and IRES (note no promoter is present);

The instant independent claims 21, 38 recite an expression vector comprising a first and

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second selection gene, and the first and second selection genes are fused, and transcription from the promoter fused to first selection gene results in a single transcript encoding the first and second selection genes, and the first selection gene is HBEGF.

The instant independent claims 25, 28 recite an expression vector comprising from 5` to 3`: HBEGF, ...., an IRES site, and a promoter of interest.

The specification discloses expression vectors comprising IL-4 inducible promoter and HBEGF. The specification discloses that by linking HBEGF gene to the promoter of interest, particularly the IL-4 ε promoter, a selection system is created. Thus, for screening for inhibitors of the promoter, cells that survive DT are inhibited in that no HBEGF is present. The specification has not disclosed the expression vectors which, do not have IL-4 ε promoter linked to HBEGF. The instant claims are silent regarding the promoter. The expression vectors with HBEGF linked with IL-4 ε promoter meets the written description. However, claims 13, 15-24, 34-45 is directed to expression vectors comprising HBEGF and a second marker, which are not disclosed in the specificaiton. Claims 25, and 28 recite that the expression vector comprises in 5` to 3`: a nucleic acid encoding HBEGF, .... GFP and a promoter of interest. These claims have no support in the specification. Neither the specification disclosure nor the figures support the instantly claimed expression vectors, in which the promoter is at 3` end, away from the HBEGF, which is at the 5` end (according to claims). The figure 18 A-B shows that the promoter is linked to the HBEGF. Thus, none of these claims meet the written description provision of 35 USC 112, first paragraph. The specification provides insufficient written description to support the genus encompassed by the claim.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of expression vectors comprising HBEGF linked to IL-4  $\epsilon$  promoter, the skilled artisan cannot envision the detailed expression vector structure of the vectors. The specification has no working examples of the vectors or the figures do not support the broadly claimed expression vectors.

University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams,

formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. *Fiers v. Revel*, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

The name cDNA is not itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA. Describing a method of preparing a cDNA or even describing the protein that the cDNA encodes, as the example does, does not necessarily describe the cDNA itself. No sequence information indicating which nucleotides constitute human cDNA appears in the patent, as appears for rat cDNA in Example 5 of the patent. Accordingly, the specification does not provide a written description of the invention of claim 5.

Therefore, only the expression vectors with HBEGF linked to IL-4 ε promoter, but not the full breadth of the claim meets the written description provision of 35 USC 112, first

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paragraph. The species specifically disclosed (expression vectors comprising HBEGF linked to IL-4 ε promoter) are not representative of the genus because the genus is highly variant.

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

18. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

19. Claims 21, 38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 21 recites the limitation "said first and second selection genes" in line 4; and "the two selection genes" in line 5. There is insufficient antecedent basis for this limitation in the claim.

Claim 38 recites the limitation "said first and second selection genes" in line 4; and "the two selection genes" in line 5. There is insufficient antecedent basis for this limitation in the claim.

20. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

21. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various

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claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

22. Claims 13, 15, 16, 17, 19, 20, 30, 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over US patent 6,465,253 B1 (Wickham et al) and US patent 6,613,563 B1 (Sosnowski et al).

The instant claim 13 recites an expression vector comprising a nucleic acid encoding HBEGF, GFP and IRES.

Wickham et al teach vectors and methods for gene transfer to cells. The reference teaches modified adenovirus vectors comprising non-native amino acid sequences. The reference teaches non-native amino acid sequence of UTV or Universal Transfer Vector sequences. The reference preferably teaches the non-native amino acid sequence or UTV sequence comprises heparin binding motifs, and a stretch of 21 amino acids of the heparin binding epidermal growth factor like growth factor (HB-EGF) (refers to the HBEGF of the instant claims). The reference teaches adenoviral vectors, which can comprise additional sequences, a protease recognition sequence (refers to 2a site of the instant claims) (e.g., see column 17). The reference teaches that the vectors comprise additional marker genes such as gene encoding GFP (refers to the second selection gene or GFP of the instant claims) (e.g., see column 19). The reference teaches that the non-coding sequences include promoter sequences.

The claimed invention differs from the prior art teachings by reciting that the expression vector comprises IRES site. Wickham et al teach adenoviral vectors comprising HB-EGF, 2a site and GFP. Wickham et al do not teach that the vectors comprise IRES site. However, Sosnowski et al teach viral vectors with modified tropism. The reference teaches adenovirus vectors comprising a targeting ligand. The reference teaches that the targeting ligand can be heparin binding growth factors, and heparin binding EGF like factor (HBEGF) (refers to the nucleic acid encoding HBEGF of the instant claims) (e.g., see column 11, column 22). The reference teaches heparin-binding epidermal growth factors (HBEGF) and DNA encoding HBEGF (e.g., see column 28). The reference teaches that the DNA sequence of the ligand is generally introduced into a plasmid in operative linkage with an appropriate promoter (refers to the promoter of interest of the instant claims) (e.g., see column 46). The reference teaches that elements that increase the expression of the desired product are incorporated into the construct, and such elements include internal ribosome binding site (IRES of the instant claims) (e.g., see column 49). Thus, it would have been obvious to one skilled in the art at the time the invention was made to use IRES site in the expression vectors such that the expression of the desired product is increased.

*Response to Arguments*

23. Applicant's arguments with respect to claims 13-45 have been considered but are moot in view of the new ground(s) of rejection.

*Conclusion*

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24. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Padmashri Ponnaluri whose telephone number is 571-272-0809. The examiner is on Increased Flex Schedule and can normally be reached on Monday through Friday between 7 AM and 3.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



PADMASHRI PONNALURI  
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Art Unit 1639

06 January 2005